Patent
Attorney's Docket No. 003300-506

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of	)	**MAILSTOP: AF**
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Ake LINDAHL et al.	)	Group Art Unit: 1617
	)	
Application No.: 09/155,642	)	Examiner: Shengjun Wang
	)	
Filed: October 2, 1998	)	Confirmation No.: 8949
	)	
For: BIOLOGICALLY ACTIVE COMPOSITION	)	

REPLY AFTER FINAL REJECTION

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In response to the Office Action mailed May 7, 2003, Applicants submit the following remarks.

As correctly stated in the Official Action, Claims 55-99 are pending in the application. Claims 59, 60, 81, 81, 83, 84, 95, 96, 98, and 99 stand withdrawn from consideration. Claims 55-58, 61-79, 82, 85, 88-94, and 97 stand rejected.

Interview Summary

Applicants gratefully acknowledge the courtesy shown by the Examiner to Applicants' undersigned representative on November 3, 2003. During the interview, the outstanding rejections under 35 U.S.C. §§ 112 and 103 were discussed. Applicants' representative presented arguments that are discussed in greater detail below under the

respective rejection headings. The Examiner did not agree with the arguments of Applicant's representative but agreed to carefully consider the arguments when presented in a response to the outstanding Office Action.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 55-58, 61-79, 82, 85, 88-94, and 97 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Specifically, the Examiner asserts that there is "double inclusion" of elements in Claim 55. This rejection is respectfully traversed.

For the sake of argument, Applicants follow the Examiner's logic and consider two scenarios: i) that the "oil having the capacity to plasticize" consists of "unsaturated ...fatty acid alcohols" (*i.e.*, that a portion of component a) and component c) of Claim 55 are identical); and ii) that the "oil having the capacity to plasticize" includes as a component, an "unsaturated ...fatty acid alcohol" (*i.e.*, commonality between ingredients of a) and c)). Both of these scenarios are supported by the specification which states that if desired, to address viscosity issues, an "oil having the capacity to plasticize" may be included in the composition. Insofar as the plasticizer is present, nowhere is it stated that it must be distinct from the solvent.

Turning to the first scenario, if there is identity between a portion of component a) and component c), the quantity of components is not indefinite, because the amount of solvent/plasticizer is simply cumulative. Moreover, it is well known in the pharmaceutical

art that excipients can often have effects or functions other than the function for which they are primarily employed.

With regard to the second scenario, one must consider that plasticizers may be complex natural mixtures, one or more ingredients of which can act as a plasticizing oil, and other ingredients that may have other functions such as a solvent effect. In fact, the specification mentions lanolin as an example of such a complex mixture. First, inasmuch as these mixtures are complex, they are nevertheless well-defined. Indeed, they must be if they are to be employed in a pharmaceutical/cosmetic formulation. It follows that, insofar as there is some commonality between the ingredients in the plasticizer and the solvent components of the presently claimed invention, the skilled person would be well-apprised of this and will be able to identify in the final composition, those ingredients that are solvents within the terms of the present invention, and those that are plasticizing oils.

Additionally, Applicants respectfully submit that the Examiner must not consider that the composition claim requires the admixture of a component a) containing 20-85% of solvent comprising unsaturated fatty alcohol in combination with an alkylene glycol, with a component c) containing 2-30% plasticizing oil. On the contrary, what is important for determining the scope of a product claim is only that in the final mixture, 20-85% by weight is an unsaturated fatty alcohol along with an alkylene glycol, and 2-30% of the composition is a plasticising oil, irrespective of whether the source of those ingredients is component a) or component c) or any other source for that matter.

During the interview with Applicants' undersigned representative, the Examiner appeared to suggest that two separate independent claims be written to encompass these scenarios, rather than currently pending Claim 55. Applicants believe such action is unnecessary. If the current claim language is clear and one skilled in the art would reasonably understand the scope of the claim, that is all that is required under 35 U.S.C. § 112, not multiple claims. Also during the interview the Examiner suggested a number of scenarios that he felt would be unclear whether they fell within the scope of the claim or not. However, Applicants' representative readily explained whether such scenarios fell within the scope of the claim or not.

The error of the Examiner's reasoning is further magnified by the fact that Claim 76 was included in this rejection. Claim 76 is a process claim in which an active agent is dissolved in a solvent in one step, and a plasticizing agent is added to the solution in a second step. It is irrelevant if a portion of the solvent and the plasticizer are identical for purposes of this process claim. A process requiring the addition of ingredients (even identical ingredients) separated by time or physically is entirely clear in its meaning and the skilled person would clearly understand the scope of such a claim.

Applicants therefore respectfully submit that the currently pending claims are in no way indefinite. Accordingly, withdrawal of this rejection is respectfully requested.

Rejections Under 35 U.S.C. § 103

Claims 55-58, 61-79, 82, 85-94, and 97 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Yamada et al. (U.S. Patent No. 5,362,497) in view of Wang et al. (U.S. Patent No. 4,299,828) and Cooper (U.S. Patent No. 4,552,872). This rejection is respectfully traversed.

The Examiner asserts that one cannot show nonobviousness by attacking the references individually. While this is true, that was not Applicants' intent in analyzing each of the references individually. Applicants have analyzed the alleged "contributions" of each publication toward the Examiner's assertion of obviousness to show why each is deficient in providing each and every element of the presently claimed invention and to demonstrate that the purposes of the various publications cited differ from each other and that of the presently claimed invention. Further, Applicants have shown why one skilled in the art would not be motivated to combine the references based on the express teachings of the same references that the Examiner believes renders the current claims obvious. Indeed, as discussed further below, the Examiner has ignored Applicants' arguments in this regard and has repeatedly discounted such teaching away found in the cited publications.

In order to establish *prima facie* obviousness under 35 U.S.C. § 103, the cited reference or combination of references must teach or suggest every element of the claims. Moreover, there must be motivation, outside of Applicants' disclosure, to modify or combine the cited references. *See* M.P.E.P. 2143 *et seq.*

Applicants have highlighted the differences between the composition of Yamada et al. and the presently claimed invention in the Reply filed June 11, 2002 (see pages 4-5). Applicants respectfully submit that Yamada et al. disclose the benefits of separating two kinds of enhancers. In contrast, the presently claimed invention results in a homogeneous composition. Yamada et al. disclose the use of certain compounds as enhancers while the presently claimed invention utilizes the compounds for solvents. In the presently claimed invention, the particular combination of ingredients allows one to obtain a homogenous phase, without the use of the super water-absorbent resin relied upon by Yamada et al. If the compounds separate into a two-phase system, as occurs in the absence of the super water-absorbent resin, the intended solubility properties will change and the one will not obtain the presently claimed invention, which is a homogeneous composition.

Further, Applicants respectfully maintain their position that Yamada et al. is irrelevant to the presently claimed invention and, in fact, teaches away from the presently claimed invention. Yamada et al. seek to avoid separation of a transdermal therapeutic composition, comprising a water-soluble and a lipid-soluble enhancer from an adhesive via the use of a water absorbent resin. See col. 2, lines 25-35. Yamada et al. explicitly state that the use of alkylene glycol and fatty acids or alcohols are incompatible (col. 1, lines 62-66). The presently claimed invention solves the incompatibility problem via specific mixtures of solvents to create a one-phase system while the solution to the problem in Yamada et al. is to utilize a superabsorbent polymer. This superabsorbent polymer is a critical element of the disclosure of Yamada et al. Applicants maintain that the skilled

artisan would not obviously appreciate that enhanced homogeneity and penetration could be generated by a formulation that does not contain adhesives and superabsorbing polymers such as those discussed by Yamada et al. Yamada et al. do no provide an enabling disclosure for the presently claimed invention, *i.e.*, Yamada et al. indicate that the problems of the prior art are overcome only with the use of the superabsorbing polymer. Thus, there is no motivation to use a composition of Yamada et al. *sans* the adhesives and superabsorbing polymers because Yamada et al. specifically highlight the problems with such a composition. In fact, such lack of motivation highlights the surprising nature of the presently claimed invention, which further supports a finding of non-obviousness.

Further, Applicants respectfully submit that the composition of Yamada et al. is intended for transdermal delivery of a therapeutic composition in order to produce the intended systemic effect (col. 1, lines 19-23 *et seq.*), while Applicants' claimed invention is directed toward the local delivery of the therapeutic ingredient to the skin. Indeed, Yamada et al. seek to achieve a pharmacologically active concentration in the bloodstream. Col. 1, lines 26-33. Applicants point to the extensive listing of systemic drugs in Yamada et al. in support of this. Col. 2, line 47 through Col. 3, line 25.

The Examiner argues that Cooper et al. teach the inclusion of a wax to impart the stiffness to the composition. Applicants acknowledge that Cooper discusses the use of wax in a composition. However, the Examiner ignores the express limitation of Cooper et al. on the amount of wax to be used in the composition. Col. 10, l. 40-42, Cooper et al. state that waxes "are capable of significantly interfering with the penetration enhancing abilities

of the present invention." Cooper et al. discuss the use of compositions for local delivery and for systemic delivery. Col. 1, l. 37-41. Cooper et al. state, "a vehicle system which increases both the level and speed of penetration of the steroid through the skin would be more efficient in the treatment of localized conditions and, more importantly, would greatly increase the chances of making systemic treatment by topical application viable." Col. 2, l. 50-55. However, in discussing waxy components, Cooper et al. conclude that, "while a certain level of such ingredients can be tolerated in a system which is otherwise particularly effective, in a preferred embodiment of the invention such ingredients are limited to less than about 10% and preferably less than 5%." (col. 10, l. 49-54). Because, as discussed above, Yamada et al. is directed to the systemic delivery of active ingredients, one skilled in the art would not be motivated to use the high percentage of wax as presently claimed, as such a choice would reduce penetration of the active ingredients.

However, the Examiner chooses to ignore this inconsistency by alleging that Wang teaches an amount of wax of 10-40% and suggests that unexpected results are necessary. Office Action, page 4. Applicants respectfully submit that the Examiner has erred by simply **picking and choosing** whichever elements of each reference support his argument and ignoring those that teach away from the presently claimed invention. This is impermissible. "A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention." *See* M.P.E.P. § 2141.02 citing *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 U.S.P.Q. 303 (Fed. Cir. 1983), *cert denied*, 469 U.S. 851 (1984) (emphasis in original).

In contrast, independent Claim 55 requires "b) a viscosity enhancing agent for imparting a solid consistency to the composition which comprises 15 to 55% by weight of a waxy substance." Thus, not only do Cooper et al. not disclose or suggest the specific limitations of the presently claimed invention, but Cooper et al. also expressly caution against using the very amounts the presently claimed invention advocates. Thus, Cooper et al. cannot be considered to render the claimed invention obvious because it expressly teaches away from the particular limitations.

The Examiner has previously argued that Wang et al. disclose that steroid containing stick compositions can be manufactured and that the active ingredient is preferably dissolved in the formulation. However, neither the disclosure of Wang et al. or of Cooper et al. render the present invention obvious. Wang et al. disclose a composition that the present specification demonstrates does not work in practice. The examples in the instant specification (as recited in independent claim 55) clearly show that if the composition contains less than 12% of alkylene glycol, the pharmaceutical activity of the formulation is very low. This is not disclosed or suggested by Wang et al. In fact, Wang et al. state that the propylene glycol (used as an antimicrobial but that also acts as a penetration enhancer) is preferably from about 2% to 10% by weight and optimally from about 3% to about 8%. Col. 3, lines 17-22. Wang et al. note that a concentration of 6% of propylene glycol kills 99.9% of bacteria. Col. 3, lines 24-29. Again, the Examiner chooses to ignore the **express teachings** of the Wang et al. publication in order to support his argument of obviousness. The Examiner asserts that "the employment of more than

12% of glycol would be obvious for both antimicrobial activity and for transdermal absorption enhance [sic]." Office Action, page 4. In light of the fact that Wang et al. disclose that 6% polyethylene glycol kills nearly all bacteria and that the optimal range is one-quarter to two-thirds of the **minimal** amount required by the presently claimed invention, there is **no motivation** in the Wang et al. publication to use **at least 12%** of polyethylene glycol. Generally, one does not use more of an ingredient than is necessary. Therefore, one skilled in the art would not be motivated to use higher concentration of propylene glycol (such as that found in the Yamada et al. publication) in a steroidal stick formulation based on the disclosure of Wang et al. Accordingly, the Wang et al. and Yamada et al. publications are incompatible.

Further, Wang et al. assert that waxes are preferably between about 10 to 40% and preferably about 15 to about 30% by weight. Col. 3, l. 13-16. As noted above, Cooper et al. expressly seek to avoid such high amounts of wax. Thus, the Cooper et al. and Wang et al. publications are incompatible and cannot be combined to render the presently claimed invention obvious. Applicants respectfully submit that the Examiner has attempted to combine references which expressly contradict the selection of certain components, without considering these express contradictions.

During the personal interview with the Examiner, Applicants' representative indicated that one skilled in the art seeking to make a composition of Wang et al. for a stick-like product solely for local delivery to treat skin conditions would not be motivated to use the composition of Yamada because the goals of these two publications are different.

The Examiner has provided no rational or compelling explanation for why one skilled in the art seeking to make a composition for systemic delivery as in Yamada et al. would turn to Wang et al. for guidance or, alternatively, when seeking to make a composition for local delivery as in Wang et al. would turn to Yamada et al.

Assuming *arguendo* that these three publications could be combined, Applicants respectfully submit that one skilled in the art would not arrive at the presently claimed invention. If one modifies the Yamada composition, a system where the polymer stabilization of a two phase enhancer system is highlighted, by adding viscosity enhancers and employing oleic alcohol, one merely obtains a two-phase matrix thickened by both waxes and a polymeric emulsion stabilizer. The Examiner has provided no motivation to use the composition of Yamada et al. in the absence of the super water-absorbent polymer, the central focus of the Yamada et al. publication. Abiding by the disclosure of Cooper et al., one skilled in the art would believe that the presence of the waxes should be restricted to less than 10%. This resulting product will have very little, if anything, in common with the presently claimed invention.

Applicants respectfully submit that the three cited publications, Yamada et al., Cooper et al., and Wang et al., do not disclose all elements of the presently claimed invention, particularly the amounts of the different components of the composition. This is expressly acknowledged by the Examiner on page 4, lines 3-6, of the Official Action. Indeed, as Applicants have shown above, the cited publications are incompatible with each other and teach away from the presently claimed invention. Moreover, in light of the

teachings of Yamada et al., the results achieved with the presently claimed invention would be surprising to one skilled in the art. Thus, none of the cited publications, either alone or in combination, render the presently claimed invention obvious. Accordingly, withdrawal of this rejection is respectfully requested.

Conclusions

From the foregoing, further and favorable consideration of the subject application are respectfully requested and such action is earnestly solicited.

If there are any questions concerning this Reply, or the application in general, the Examiner is respectfully requested to telephone Applicants' undersigned representative so that prosecution may be expedited.

Respectfully submitted,

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Date: November 5, 2003

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